REMARKS

This responds to the Office Action mailed on November 29, 2006.

Claims 5, 6 and 19 are cancelled and claims 21 and 22 are added. As a result, claims 1-3, 7-10, 12-18 and 20-22 are now pending.

Support for the subject matter of claim 21, relating to reduction or termination of anti-viral treatment after administration of the recombinant poxvirus is found throughout the specification, for example, at page 5, lines 23-27, and in the Examples and figures (see, e.g., Fig. 7). Support for the subject matter of claim 22, relating to interruption of anti-viral treatment after administration of the recombinant poxvirus is found throughout the specification, for example, in Example 6 at page 26 and Fig. 8.

Claims 1, 7, 8, 9, 12, 18, and 20 are amended. The language of claims 1, 18 and 20 has been modified to specify that the peptides are presented in an amount sufficient to stimulate HIV "antigen-specific CD8+ and CD4+ responses." Support for stimulation of HIV "antigen-specific CD8+ and CD4+ responses" is found throughout the specification, for example, in the Examples (see especially, Figures 1-4; page 18, line 24 to page 21, line 28; page 25, lines 11-15; page 20, lines 25-27). Moreover, "an attenuated recombinant poxvirus" is administered in claims 1, 9, 18 and 20. Support for use of an attenuated recombinant poxvirus can be found throughout the specification and claims as originally filed, for example, in original claims 5 and 6. Language relating to "vaccine" has been deleted from claim 12 and the dependencies of claims 7 and 8 have also been amended.

Applicant submits that no new matter has been added to the specification or claims.

§112 Rejection of the Claims

Claims 1-3, 5-10 and 12-20 were rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate description or enablement. The Examiner has alleged that the specification does not enable the following aspects of the claimed invention.

Immunogens capable of inducing a protective HIV-specific CD8+ immune response

The Examiner has alleged that the specification does not enable immunogens capable of inducing a protective HIV-specific CD8+ immune response. The pending claims are directed to methods of stimulating a HIV1-specific $CD8^+$ response by using a recombinant poxvirus to express peptides in an amount sufficient to stimulate a $CD8^+$ HIV antigen-specific response. Language relating to a protective HIV-specific CD8+ response is not present in the pending claims. In addition, contrary to the Examiner's allegations, the claims are directed to specific immunogens -- HIV specific peptides including HIV Gag, Gp120, Env, Nef or Pol peptides.

Moreover, Applicant submits that the specification clearly enables the claimed invention. In particular, for example, as shown in FIG. 2 and as described in the specification at page 18, line 24 to page 21, line 28, anti-viral agent treated animals who were inoculated with a recombinant NYVAC that produces gag-pol-env HIV specific peptides (Group B), exhibited substantially increased percentages of HIV-specific $CD8^+$ T cells relative to anti-viral agent treated animals that received a placebo vaccine (Group A) or animals inoculated with the recombinant NYVAC virus who had received no anti-viral agent treatment (Group C). Thus, as the specification discloses at page 22, lines 8-10, the inventive methods induced significant expansion of the number of CD8+/CD3+ cells specific for an immunodominant gag peptide only in animals treated effectively with antiretroviral therapy (i.e., both anti-retroviral agents and the recombinant NYVAC virus that produces gag-pol-env HIV specific peptides).

Guidance as to the correlates of human protection

The Examiner asserts that the specification does not provide guidance on the correlates of human protection and states that the specification fails to address the suggested need for both polyfunctional (IL-2 and IFN-γ) CD4+ and viral-specific CD8+ T-cell responses.

Applicant submits that the present claims are directed to method of stimulating a HIV1-specific $CD8^+$ response, and that the terms "protection" and "prevention" are not used in the claims.

Moreover, Applicant submits that the Examiner's allegations that the specification fails to disclose that both CD4+ and CD8+ responses are induced by the present methods is untrue. In fact, the specification provides data (FIG. 1) showing that gp120-specific CD4+ T cell proliferation was significantly increased in animals that received both anti-retroviral agents and

the recombinant NYVAC virus that produces gag-pol-env HIV specific peptides (Group B). The application further discloses that proliferative CD4+ responses to p27 Gag and gp120 were increased by NYVAC gag-pol-env vaccination up to three- and twelve-fold (page 25, lines 11-15). Moreover, the specification explicitly discloses that "These data provide the first evidence that a highly attenuated live recombinant poxvirus vaccine can induce and boost sustained CD4+ helper immune response in the context of a pharmacologically controlled lentiviral infection" (page 20, lines 25-27).

Furthermore, in recognition that the immunomodulatory molecule IL-2 can improve the CD4+ and CD8+ responses, the specification explicitly teaches that IL-2 can be administered at the same time as the recombinant poxvirus (see Example 6, page 24, line 31 to page 26, line 13). The specification teaches that such administration of IL-2 at the same time as the recombinant poxvirus is administered "potentiated and broadened CD8+ T-cell functional responses" (page 26, lin3w 1-2). Further the specification discloses "expanded CD8+ (top panel, Figure 8) and CD4+ proliferative (lower panel, Figure 8) responses" upon administration of the NYVAC gag-pol-env recombinant virus with low doses of IL-2 (page 26, lines 4-13).

Accordingly, the inventive methods clearly stimulate CD4+ and CD8+ responses and Applicant respectfully requests withdrawal of this rejection.

Quasispecies nature of HIV

The Examiner alleges that the HIV-1 genome is plastic and contributes to immune escape, asserting that the specification fails to provide guidance concerning the identification of epitopes that are resistant to viral escape.

Applicant submits that the invention is drawn to a use of variety of epitopes (not one single antigenic peptide) to optimally stimulate the immune system against a variety of viral antigens and thereby minimize the probability of escape. As the specification discloses, "Following therapy suspension, NYVAC-SIV-vaccinated animals were able to control viremia better than animals treated with antiretroviral therapy alone." The present methods are clearly therapeutically beneficial.

Applicant respectfully requests withdrawal of this rejection.

Working Examples

Applicant reminds the Examiner that a Declaration by Dr. Franchini has previously been submitted on May 16, 2005 that describes two clinical trials conducted by Aventis Pasteur as well as proposed clinical trials by EuroVacc. The clinical trials involved administration of a recombinant pox virus that encoded HIV peptides (vCP1452) to human HIV-infected patients. In the ACTG5054 Trial, the patients had been undergoing antiretroviral therapy (ART) and prior to administration of vCP1452 had a median CD4 count of 609 and a viral load of less than 50 (see pages 3 and 5 of the Declaration Appendix). Preliminary results indicated that patients who received the recombinant vCP1452 pox virus alone had a lower viral load than those who received placebo (page 5 of the Declaration Appendix)). In the Quest trial, patients who received the recombinant pox virus had increased CD4 and CD8 responses at week 24 (see page 11 of the Declaration Appendix).

A press release by EuroVacc, which was provided with the Supplemental Information Disclosure Statement filed in May 2005, describes results from a NYVAC-HIV C vaccine trial. *See* article entitled, "Results from EV01 HIV Vaccine Trial, London and Lausanne, July 7th, 2004." The vaccine employed a highly attenuated recombinant vaccinia virus that expresses *gag*, *pol*, *nef* and *env* synthetic genes of HIV-1 clade C. *Id.* As reported, the vaccine was well-tolerated by the 24 people who received it. *Id.* Vaccine-induced anti-HIV T-cell responses were observed in 5/12 (45%) of the vaccine recipients using stringent quality controlled clinical lab assays. *Id.* *Env*-specific responses were found in all 5 responding subjects but additional responses against other proteins of HIV (e.g. Gag and Nef) were detected in 40% of the responders. *Id.* Anti-env antibodies, analyzed at the University of Oxford, were detected in 5/24 (20%) of volunteers at week 4. *Id.* Hence, administration of recombinant pox viruses can stimulate CD4 and CD8 responses.

State of the art

The Examiner asserts that not one single effective HIV CTL vaccine is on the market and undue experimentation would be required to identify vaccines that would have long-lasting and high titer immune responses.

Applicant submits that the specification fully enables one of skill in the art to make and use the inventive methods to stimulate CD4 and/or CD8 responses. Moreover, the claim language of the pending claims explicitly states what the present methods can do (stimulate CD4 and/or CD8 responses). Language relating to "vaccines" is not present in the claims.

Moreover, while the Examiner has cited several articles and letters in an effort to illustrate the unpredictability of HIV vaccine technology, Applicant notes that several of these articles are five or more years old. Hence, the current state-of-the-art may not reflect as much uncertainty as the Examiner alleges. In addition, Applicant submits that the Examiner's failure to find effective methods of stimulating a CD8+ response in the prior art merely serves to illustrate the novelty and non-obviousness of the claimed invention.

Thus, Applicant submits that the claimed invention is fully enabled by the specification and respectfully requests withdrawal of this rejection under 35 U.S.C. §112, first paragraph.

Reservation of Rights

In the interest of clarity and brevity, Applicant may not have addressed every assertion made in the Office Action. Applicant's silence regarding any such assertion does not constitute any admission or acquiescence. Applicant reserves all rights not exercised in connection with this response, such as the right to challenge or rebut any tacit or explicit characterization of any reference or of any of the present claims, the right to challenge or rebut any asserted factual or legal basis of any of the rejections, the right to swear behind any cited reference such as provided under 37 C.F.R. § 1.131 or otherwise, or the right to assert co-ownership of any cited reference. Applicant does not admit that any of the cited references or any other references of record are relevant to the present claims, or that they constitute prior art. To the extent that any rejection or assertion is based upon the Examiner's personal knowledge, rather than any objective evidence of record as manifested by a cited prior art reference, Applicant timely objects to such reliance on Official Notice, and reserves all rights to request that the Examiner provide a reference or affidavit in support of such assertion, as required by MPEP § 2144.03. Applicant reserves all rights to pursue any cancelled claims in a subsequent patent application claiming the benefit of priority of the present patent application, and to request rejoinder of any withdrawn claim, as required by MPEP § 821.04.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (516) 795-6820 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 28TH day of March 2007.

KIMBERLY BROWN

Name

Signature